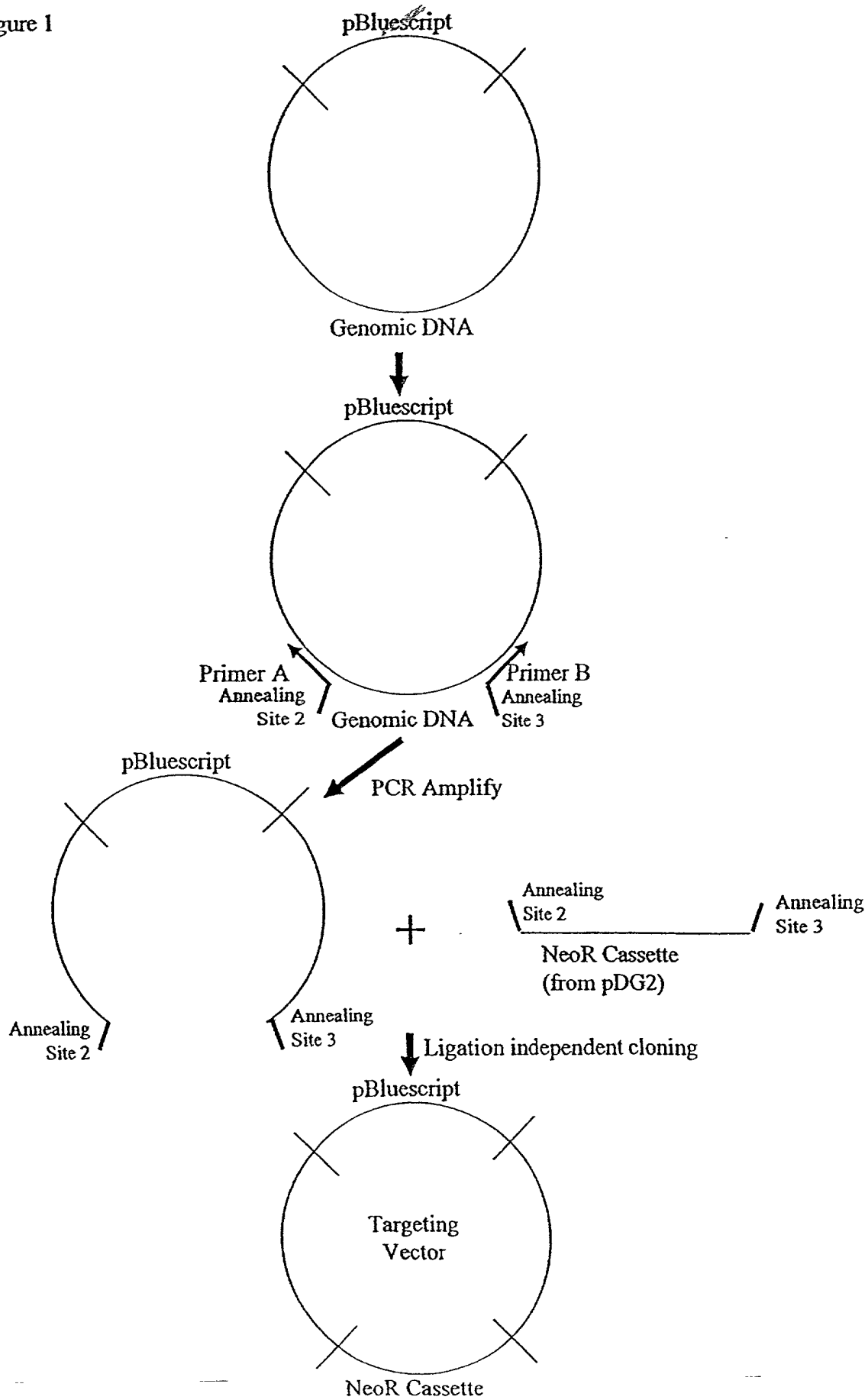


Figure 1



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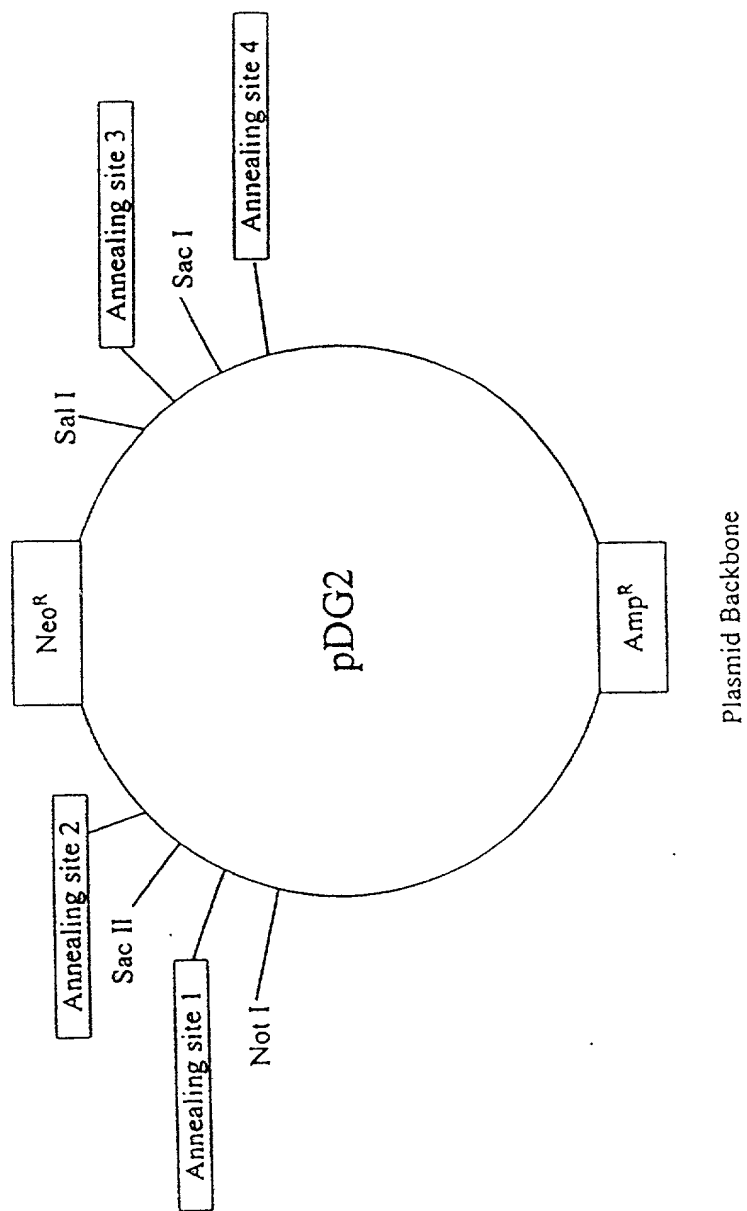


FIGURE 2A

FIGURE 2B

pDG2:

GTAACTACGTCAGGTGGCACTTTTCGGGGAAATGTGCGGGAACCCCTATTGTTTATTTTCTAAATACATTCAAATA  
TGTATCCGCTCATGAGACAATAACCCGTGATAAATGCTTCAATAATATTGAAAAAGGAAGAGTATGAGTATTCAACATTTTC  
CGTGTGCGCCTTATTCCTTTTTTTCGGGCATTTTGCCTTCTGTTTTTGTCTACCCAGAAACGCTGGTGAAAGTAAAGA  
TGCTGAAGATCAGTTGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAAGATCCTTGAGAGTTTTTCGCC  
CCGAAGAACGTTCTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGTATTATCCCGTGTGACGCCGGGCAA  
GAGCAACTCGGTGCGCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCAAGAAAAGCATCTTACGGA  
TGGCATGACAGTAAGAGAATTATGCAGTGTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGA  
TCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACCTGCGCTTGATCGTTGGGAACCGGAG  
CTGAATGAAGCCATACCAAACGACGAGCGTGACACCAAGATGCTGTAGCAATGGCAACAACGTTGCGCAAACTATTAAAC  
TGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACTTCTGC  
GCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGACAG  
CTGGGGCCAGATGGTAAGCCCTCCGCTATCGTAGTTATCTACACGACGGGGAGTCAAGCAACTTGGATGAACGAAATAG  
ACAGATCGCTGAGATAGGTGCCTCACTGATTAAAGCATTGGTAACCTGTCAGACCAAGTTTACTCATATATACTTTAGATTG  
ATTTACCCCGGTTGATAATCAGAAAAGCCCCAAAAACAGGAAGATTGTATAAGCAAATATTTAAATTGTAAACGTTAATA  
TTTTGTTAAATTCGCGTTAAATTTTTGTTAAATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAAAATCCCTTAT  
AAATCAAAGAATAGCCCGAGATAGGGTTGAGTGTGTTCCAGTTTGGAAACAAGAGTCCACTATTAAGAACCGTGGACTC  
CAACGTCAAAGGGCGAAAAACCGTCTATCAGGGCGATGGCCCACTACGTGAACCATCACCCAAATCAAGTTTTTTGGGGT  
CGAGGTGCGTAAGCACTAAATCGGAACCTTAAAGGGAGCCCCGATTAGAGCTTGACGGGGAAGCGAACGTGGCGA  
GAAAGGAAGGGAAGAAAGCGAAGGAGCGGGCGCTAGGGCGCTGGCAAGTGTAGCGGTCAAGCTGCGCGTAACCAACACA  
CCCCCGCGCTTAATGCGCGCTACAGGGCGCTAAAGGATCTAGGTGAAGATCCTTTTGATAATCTCATGACCAAAA  
TCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTT  
CTGCGCGTAATCTGCTGCTTGCAACAAAAAACCCAGCTACCAGCGGTGGTTTGTGTCGGATCAAGAGCTACCAAC  
TCTTTTTTCGAAGGTAACCTGGCTTCAGCAGAGCGCAGATACCAATACCTGTTCTTCTAGTGTAGCCGTAGTTAGGCCACC  
ACTTCAAGAACTCTGTAGCACCGCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAG  
TCGTGCTTACCGGGTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTGCGGCTGAACGGGGGGTTCGTGCAC  
ACAGCCAGCTTGAGCGAAGCACTACACCGAAGTGAATACCTACAGCGTGAAGTATGAGAAAGCGCCACGCTTCCCG  
AAGGGAGAAAGGCGGACAGGTATCCGTTAAGCGGCAGGTCGGAACAGGAGCGCACGAGGGAGCTTCCAGGGGAAAC  
GCCTGGTATCTTTATAGTCTGTGCGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCG  
GAGCCTATGGA AAAACGCCAGCAACGCGGCTTTTTACGGTTCTGCGCTTTTGTGCTGCTTTTGTCTACATGTAATGTG  
AGTTAGCTCACTCATTAGGCACCCAGGCTTTACACTTTATGCTTCCGGCTCGTATGTTGTGTGGAATTGTGAGCGGATA  
ACAAATTTACACAGGAAACAGCTATGACCATGATTACGCCAAGTACGTAATACGACTCACTAGGCGGCGCGTTTAAAC  
AATGTGCTCCTCTTTGGCTTGCTTCCGCGGGCAAGCCAGACAAGAACAGTTGACGTCAAGCTTCCCGGACCGCTGTCT  
AGCGCGCGCGCAATTCCGTGAGGATTCGAGGGCCCTGACGGTCAATCTACCGGTAGGGGAGGCGCTTTCCCAAGG  
CAGTCTGGAGCATGCGCTTAGCAGCCCGCTGGCACTTGGCGCTACACAAGTGGCCTCTGGCTCGCACATTCCACA  
TCCACCGGTAGCGCAACCGGCTCCGTTCTTGGTGGCCCTTTCGCGCACCTTCTACTCTCCCTAGTCAGGAAGTTC  
CCCCCGCGCGCAGCTCGCGTCTGTCAGGACGTGACAAATGGAAGTAGCACGTCTCACTAGTCTCGTGAGATGGACAG  
CACCGCTGAGCAATGGAAGCGGTAGGCCCTTGGGGCAGCGGCAATAGCAGCTTGTCTCTTCTGCTTTCTGGGCTCAGA  
GGCTGGGAAGGGTGGGTCCGGGGCGGGCTCAGGGCGGGCGGGCGGAGGCTCTCCGAGGCCCC  
GGCATTCTCGCAGCTTCAAAGCGCACGTCTGCCCGCTGTTCTCTCTCTCATCTCCGGGCTTTCGACCTGACG  
CAATATGGGATCGGCCATTGAACAAGATGGATTGCAACGAGGTTCTCCGGCGCTTGGGTGGAGAGGCTATTCCGCTATG  
ACTGGGCACAAACAGACAATCGGCTGCTGATGCCGCGGTGTTCCGGCTGTGAGCGCAGGGGCGCCCGTCTTTTTGTG  
AAGACCGACCTGTCCGGTGCCTGAATGAAGTGCAGGACGAGGACGCGCGCTATCGTGGCTGGCCACGACGGGCGTCC  
TTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGAAGTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCC  
TGTCATCTCACCTTGCTCTGCGGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGTGCATACGCTTGTACCGGCT  
ACCTGCCCCATTGACCAACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCGGCTTGTGTCGATCAGGA  
TGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCGCAACTGTTCCGCGAGGCTCAAGGCGCGCATGCCGACGCGCATG  
ATCTCGTCTGACCCATGGCGATGCTGCTTGCAGCAATATCATGGTGGAAAAATGGCCGCTTTTCTGGATTTCATGACTGT  
GGCCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATG  
GGCTGACCGCTTCTCGTGTCTTACGGTATCGCGCTCCCGATTGCGAGCGCATCGCTTCTATCGCTTCTTGACGAGT  
TCTTCTGAGGGGATCGATCCGCTCTGTAAGTCTGCAGAAATTTGATGATCTATTAACAATAAAGATGTCCACTAAAATGG  
AAGTTTTCTCTGCATACCTTTGTTAAGAAGGGTGAGAACAGAGTACCTACATTTGAATGAAGGATTGGAGCTACGGGG  
GTGGGGGTGGGGTGGGATTAGATAAATGCCTGCTCTTACTGAAGGCTCTTACTATTGCTTTATGATAATGTTTCATAG  
TTGGATATCATATTTAAACAAGCAAAACCAAAATTAAGGGCCAGCTCATTCTCCCACTCATGATCTATAGATCTATAGA  
TCTCTCGTGGGATCATTGTTTTCTCTTGATTCCCACTTTGTGGTTCTAAGTACTGTGGTTTCAAATGTGTCAGTTTCA  
TAGCCTGAAGAACGAGATCAGCAGCCTCTGTTCCACATACACTTCACTTCTAGTATTGTTTTGCCAAGTTCTAATTCAT  
CAGAAGCTGACTCTAGATCTGGATCCGGCCAGCTAGGCCGTGACCTCGAGTGATCAGGTACCAAGGCTCTCGCTCTGTG  
TCCGTTGAGCTCGACGACACAGGACACGCAATTAATTAAGGCCGGGCGTACCCTCTAGTCAAGGCTTAAGTGAGTCTG  
TATTACGAGTGGCCGCTGTTTTACACGTCGTGACTGGGAAAACCTGGCGTTACCAACTTAATCGCCTTGCAGCACA  
TCCCCCTTTCGCGAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTCGCGAGCCTGAATGGCG  
AATGGCGCTTCTGTTGTAATAAAGCCCGCTTTCGGCGGCTTTTTTTT

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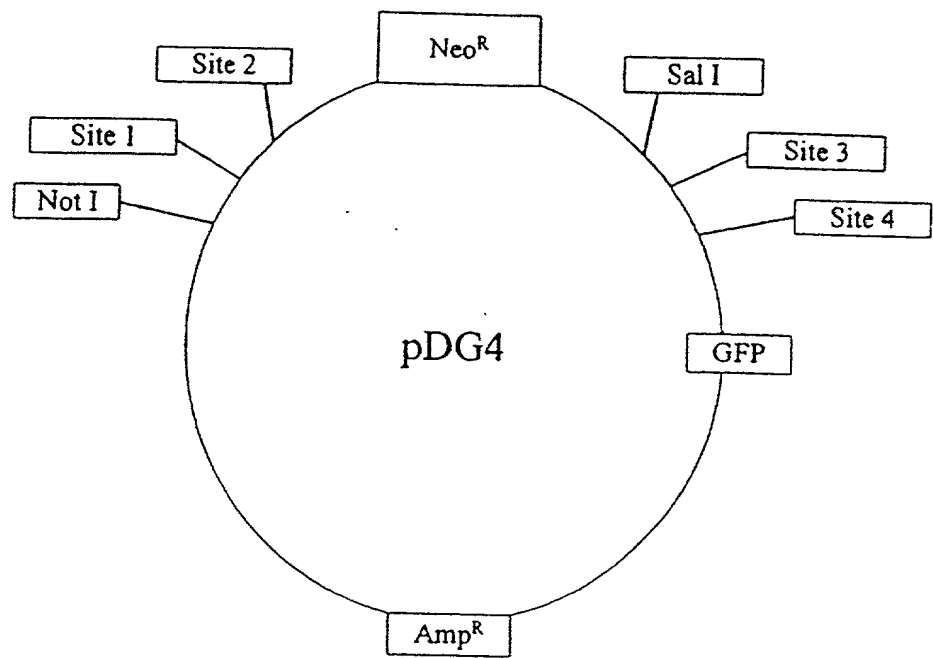


FIGURE 3A

[illegible]

TGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCCGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCG  
ACCACCAAGCGAAACATCGCATCGAGCGAGCACGTA CTGGATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAA  
GAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCCGCCAGGCTCAAGGCGCGCATGCCGACGGCGATGATCTCGTCCTGAC  
CCATGGCGATGCTGCTTGCCGAATATCATGGTGAAAAATGGCCGCTTTTCTGGATT CATCGACTGTGGCCGGCTGGGTG  
TGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTC  
CTCGTGCTTTACGGTATCGCCGCTCCCGATTCCGAGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGAGGGGA  
TCGATCCGTCCTGTAAGTCTGCAGAAATTGATGATCTATTAAACAATAAAGATGTCCACTAAAATGGAAGTTTTCCTGT  
CATACTTTGTTAAGAAGGTGAGAACAGAGTACCTACATTTTGAATGGAAGGATTGGAGCTACGGGGGTGGGGGTGGGGT  
GGGATTAGATAAATGCCTGCTCTTTACTGAAGGCTCTTTACTATTGCTTTATGATAATGTTTCATAGTTGGATATCATAA  
TTTAAACAAGCAAAACCAAATTAAGGGCCAGCTCATTCTCCCACTCATGATCTATAGATCTATAGATCTCTCGTGGGAT  
CATTGTTTTTCTCTTGATTCCCACTTTGTGGTTCTAAGTACTGTGGTTTCCAAATGTGTCAGTTTCATAGCCTGAAGAAC  
GAGATCAGCAGCCTCTGTTCCACATACACTTCATTCTCAGTATTGTTTTGCCAAGTTCTAATTCATCAGAAGCTGACTC  
TAGATCTGGATCCGGCCAGCTAGGCCGTCGACCTCGAGTGATCAGGTACCAAGGTCCTCGCTCTGTGTCCGTTGAGCTCG  
ACGACACAGGACACGCAAATTAATTAAGGCCGGCCCGTACCCTCTAGTCAAGGCCTTAAGTGAGTCGTATTACGGACTGG  
CCGTCGTTTTACAACGTCGTGACTGGGAAAACCTGGCGTTACCCAACTTAATCGCCTTGACGACATCCCCCTTTCGCC  
AGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGGCGCTTCGC  
TTGGTAATAAAGCCCGCTTCGGCGGGCTTTTTTTTT

FIGURE 3B (Continued)

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Annealing site	Sequence	Sequence after digestion
1	5' tgtgctcctctttggcttgcttccaa... 3' 3' acacgaggagaaaccgaacgaaggtt... 5'	5' tgtgctcctcttttggttgcttccaa... 3' 3' tt... 5'
2	5' ctgggttcttgcttggttggtcccaa... 3' 3' gaccaagaacagaccgaaccgggtt... 5'	5' ctgggttcttgcttggttggtcccaa... 3' 3' tt... 5'
3	5' ggtcctcgtctctgtgtccgttgaa... 3' 3' ccaggagcgagacacaggcaactt... 5'	5' ggtcctcgtctctgtgtccgttgaa... 3' 3' tt... 5'
4	5' ttgcggtgtcctgtgtcgtcgaa... 3' 3' aaacgcacaggacacagcagctt... 5'	5' ttgcggtgtcctgtgtcgtcgaa... 3' 3' tt... 5'

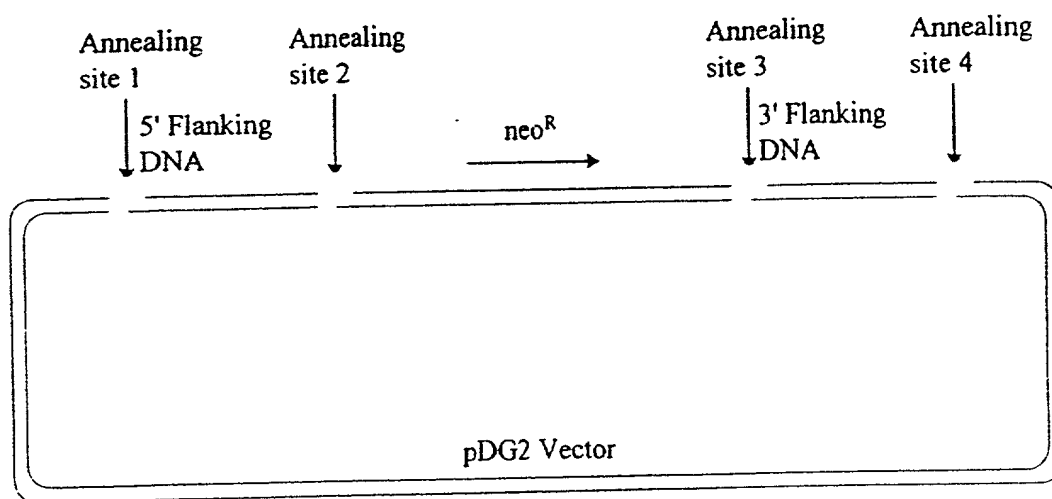
FIGURE 4

Annealing site	Sequence	Sequence after digestion
1	5' AAtgtgctcctcttcttggcttgcttCCGC 3' 3' Ttacacgaggagaaaccgaacgaagg 5'	5' AA 3' 3' Ttacacgaggagaaaccgaacgaagg 5'
2	5' AActgggttcttctgtctggcttgCCCCGC 3' 3' Ttgaccaagaacagaccgaaccggg 5'	5' AA 3' 3' Ttgaccaagaacagaccgaaccggg 5'
3	5' AAggtcctcgctctgtgtccgttgAGCT 3' 3' Ttccaggagcgagacacaggcaac 5'	5' AA 3' 3' Ttccaggagcgagacacaggcaac 5'
4	5' AAttgctgtcctctgtgtcgtcGAGCT 3' 3' Ttaaacgcacaggacacagcagc 5'	5' AA 3' 3' Ttaaacgcacaggacacagcagc 5'

FIGURE 5

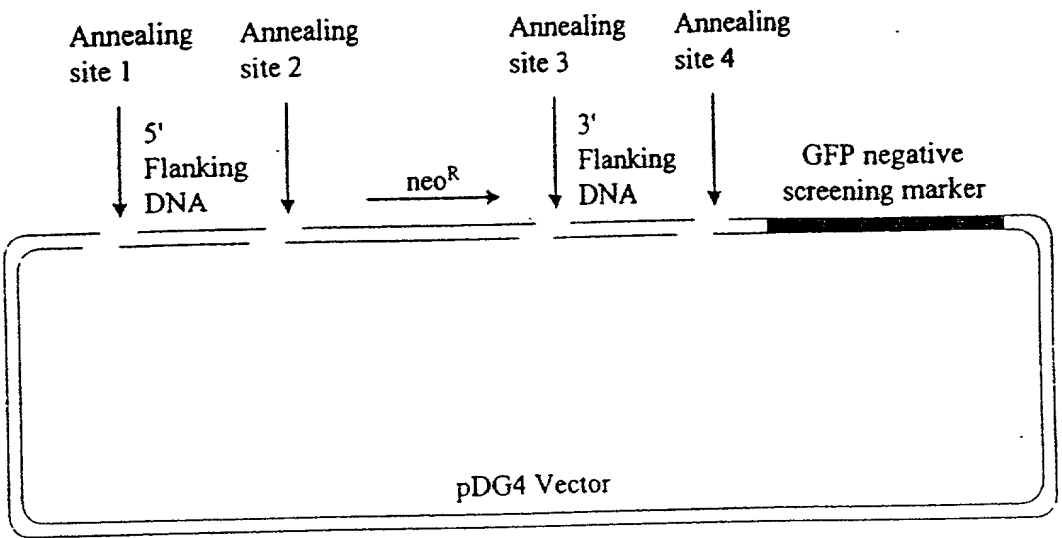


FIGURE 6



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FIGURE 7



TCCCCACATTGCAAAGCCTACACAAAGATCCCTACCACTGAGCACCGAGGGAGGCATGGCTCAGAACCCC  
 AGCAACATGGAGCCCTTGCCTAAACCACTGGTGCCTGTGAAGGGAATCCCACTCATCAAATACTTTGCGG  
 AGACAATGGAGCAACTGCAGAACTTCACAGCCTGGCCTGATGATGTGCTCATCAGCACGTACCCAAAGTC  
 TGGTACTAACTGGATGAGTGAGATCATGGATATGATCTATCAGGGTGGCAAGCTAGATAAGTGTGGCCGG  
 GCCCCCGTCTATGCCCGGATAACCTTCCTTGAGTTCAGCTGCCCAGGGGTCCCCCAGGTCTTGAAACTC  
 TGAAAGAGACACCAGCCCCACGGATCATTAAAGACACATCTGCCCTTGTCTTACTCCCTCAGAGTCTGCT  
 GGATCAAAAGATCAAGGTGATCTACGTTGCCCCGAAATGCAAAGGATGTGGTTGTCTCTATTATAACTTC  
 TACAAAATGGCCAAGCTGCACCCTGACCCAGGCACCTGGGAAAGCTTCTTGAGAACTTCATGGATGGGA  
 AAGTGTCTTATGGGTCTGGTACCAGCACGTGAAGGAGTGGTGGGAGCTGAGACGCACTCACCTGTTCT  
 CTATCTCTTCTATGAAGACATGAAGGAGAATCCCAAAGGGAGATCAAGAAGATTCTAGAGTTTCTGGGG  
 CGCTCTCTACCTGAGGAGACTGTGGATTAAATTGTTTACCACACATCCTTCAAGAAAATGAAGGAGAACC  
 CCATGGCTAACTACACAACCATCCCACTGAAGTTATGGACCACACTATTTATCCCTTCATGAGGAAAGG  
 TACCATTGGGGACTGGAAAAATACCTTCACTGTAGCCCAGAGTGAGCACTTTGATGCCCACTATGCCAAG  
 CTAATGACAGGTTGTGACTTCACGTTCCGCTGTCAAATATGAATTGTGGATATGGCTATACTGGGAACCA  
 AGGCAAGCTGACACATCCCCATCATGATCTCAAGAGAAAAATGTGATGTGTTTATATTGTTGTATGCCT  
 AAAGGAAATCTGAGCTAAGAGAATAGGACTGGGATGTAGCTGAGGCAGAGGGTCTTATGAACATGTGAG  
 AAAGCCATCAGTCCTAACACTGAAAAAGAACCTAAAGTACAAACATGCAAAAATAGTAAGATAAACTGTA  
 TTTTACCTGAACAAATAAATGCCACTGGGAGCTGACTGG

(SEQ ID NO: 19)

**Targeting Vector (5' arm; 200 bp flanking neo insert):**

AGAACCCTGCCCTACTCCACCTCCTCCCCTTTTTGTTTCTGGAGAACAGCCAGTCCTAG  
 CACTGTTTCCACTTCCTCCCACTTGGGACACAAAATCTCCAGCTCAAAGACCAATTCTG  
 CATTCCCCACATTGCAAAGCCTACACAAAGATCCCTACCACTGAGCACCGAGGGAGG  
 CATGGCTCAGAACCCAGCAACATG

(SEQ ID NO: 20)

**Targeting Vector (3' arm; 200 bp flanking neo insert):**

AGGGTGGCAAGCTAGATAAGTGTGGCCGGGCCCCCGTCTATGCCCGGATACCTTCC  
 TTGAGTTCAGCTGCCAGGGGTCCCCCAGGTATGTGCATGGGGGTGCTAGAGACAA  
 GTGGAAAAAGGTAGGACCGGGCCCCAGTTTAAACAAAGTTCCTTGTTCAACTTAGGTCT  
 TGAAACTCTGAAAGAGACACCAGCCCCA

(SEQ ID NO: 21)

FIG. 8